Sleep-Wake Cycle II
Neural Mechanisms

Reading:
BCP Chapter 19
People typically sleep about 8 hours per day, and spend 16 hours awake. Most people sleep over 175,000 hours in their lifetime.

The vast amount of time spent sleeping suggests that sleep has a significant biological function.

- recuperation
- adaptation

Sleep-Wake Cycle
Three Physiological Measures of Sleep

Electroencephalogram (EEG)
Reveals gross electrical activity of the brain “brainwaves”

Electrooculogram (EOG)
Records eye movements seen during rapid eye movement (REM) sleep

Electromyogram (EMG)
Detects muscles activity
Four Stages of Sleep EEG

Awake: low-voltage, high-frequency (fast) waves

Sleep: voltage increases and frequency decreases (slows) with progression through stages 1-4
- Stage 1: theta waves
- Stage 2: theta waves plus spindles and K complexes
- Stage 3: occasional delta waves (large and slow, 1-2Hz)
- Stage 4: predominantly delta waves
A sleeper progresses from stage 1 to stage 4 sleep and then back through stages 3, 2, to (emergent) stage 1, then repeats the cycle.

Emergent stage 1 differs from initial stage 1 (and all other stages):
- rapid eye movement (REM) sleep – dreams
- loss of body core muscle tone
- cerebral activity increases to awake levels

Sleepers progress through sleep stages in 90-minute cycles, where the durations of emergent stage 1 periods lengthen and stages 3-4 shorten as the night progresses.
REM Sleep and Dreaming

80% of awakenings from REM sleep yield reports of story-like dreams. Only 7% of awakenings from non-REM sleep lead to dream recall.

External stimuli may be incorporated into dreams.

Dreams run in “real” time.

Everyone dreams.

Interpretation?
• troubled subconscious
• activation-synthesis theory

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Why Do We Sleep?

There are two kinds of theories for sleep: recuperation and adaptation.

- Recuperation: sleep is needed to restore homeostatic balance lost during the day.
- Adaptation: sleep is the result of an internal timing mechanism, evolved to conserve energy and to protect us from the dangers of the night.

Comparative analysis:

- All mammals and birds sleep; dolphins sleep with half of their brain at a time.
- There is no clear relationship between species’ daily activity levels and sleep duration.

<table>
<thead>
<tr>
<th>Mammalian Species</th>
<th>Hours of Sleep per Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Giant sloth</td>
<td>20</td>
</tr>
<tr>
<td>Opossum, brown bat</td>
<td>19</td>
</tr>
<tr>
<td>Giant armadillo</td>
<td>18</td>
</tr>
<tr>
<td>Owl monkey, nine-banded armadillo</td>
<td>17</td>
</tr>
<tr>
<td>Arctic ground squirrel</td>
<td>16</td>
</tr>
<tr>
<td>Tree shrew</td>
<td>15</td>
</tr>
<tr>
<td>Cat, golden hamster</td>
<td>14</td>
</tr>
<tr>
<td>Mouse, rat, gray wolf, ground squirrel</td>
<td>13</td>
</tr>
<tr>
<td>Arctic fox, chinchilla, gorilla, raccoon</td>
<td>12</td>
</tr>
<tr>
<td>Mountain beaver</td>
<td>11</td>
</tr>
<tr>
<td>Jaguar, vervet monkey, hedgehog</td>
<td>10</td>
</tr>
<tr>
<td>Rhesus monkey, chimpanzee, baboon, red fox</td>
<td>9</td>
</tr>
<tr>
<td>Human, rabbit, guinea pig, pig, dolphin</td>
<td>8</td>
</tr>
<tr>
<td>Gray seal, gray hyrax, Brazilian tapir</td>
<td>6</td>
</tr>
<tr>
<td>Tree hyrax, rock hyrax</td>
<td>5</td>
</tr>
<tr>
<td>Cow, goat, elephant, donkey, sheep</td>
<td>3</td>
</tr>
<tr>
<td>Roe deer, horse</td>
<td>2</td>
</tr>
</tbody>
</table>
Effects of Sleep Deprivation

The optimal duration of sleep is unknown [i.e., there are no consistent differences in any measures of behavior or health between long (>8 hours) and short sleepers (<6 hrs)]. However, the recuperation theory of sleep predicts that individuals experiencing longer (for them) periods of wakefulness will result in behavioral/physiological disturbances, and much of the missed sleep will be regained.

In support of theory:
• bad mood, reduced cognitive abilities (creative thinking) and sleepiness
• reduced immune function, increased blood pressure, and lower body temperature

Inconsistent with the theory:
• unimpaired logical and critical thinking
• retained physical strength and motor performance
• recovery sleep is relatively short

If REM-sleep alone is deprived then the effects are minimal, indicating that deep sleep is responsible for most benefits of sleep. REM-sleep may improve memory-storage (inconclusive), or prepare an organism for wakefulness where immediate activity may be required upon waking (default theory).
Sleep-Wake Areas

There are four areas of the brain known to be directly involved in producing or reducing sleep: two in the hypothalamus; and two in the reticular formation.

- anterior hypothalamus – sleep
- posterior hypothalamus – wakeful
- rostral reticular formation – wakeful
- caudal reticular REM nuclei – sleep
The hypothalamus contains two primary sleep-wake centers: one anterior area and one posterior area.

The anterior sleep area is the ventrolateral region of the preoptic nucleus (VLPO). It inhibits its targets using GABA as its neurotransmitter.

The posterior awake area is the lateral hypothalamic area (LHA). It excites its targets using the neuropeptide orexin as its transmitter.
The reticular formation (RF) contains two primary sleep-wake centers: rostral and caudal.

The rostral RF is a wakeful center, and consists of a number of areas including:

- histaminergic (HA) tuberomammillary nucleus
- dopaminergic (DA) ventral tegmental area
- serotonergic (5-HT) Raphe nuclei
- noradrenergic locus coeruleus (LC)

The diffuse modulatory systems in rostral RF affect many functions (in addition to regulating the sleep-wake cycle), but do have certain principles in common:

- core number of neurons is small (~thousands)
- axons project widely throughout cortex
- synapses release transmitter into the extracellular fluid to affect many neurons (~100,000)
- G-protein coupled receptors
Rostral Reticular Formation 2

Thalamic neurons at rest (during sleep) tend to generate slow, delta frequency rhythms of intrinsic firing. Under the influence of neuromodulators, the neurons depolarize and switch to a more excitable single-spiking mode (resembling wakeful state).
Caudal Reticular Formation

The caudal RF is a sleep center, and consists of a number of areas that regulate different aspects of REM sleep. They are under the control predominantly of the cholinergic pedunculopontine (PPN) and laterodorsal tegmental (LDT) nuclei (which initiate ponto-geniculate-occipital cortex (PGO) waves).
Human sleep is believed to be regulated by two basic neural processes:
- the homeostatic process (sleep need), whose magnitude depends on the amount of prior sleep and wakefulness;
- the circadian process (sleep urge), which is governed by the SCN clock.

The sleep/wake cycle is thought to be governed by a flip-flop neural circuit involving mutual inhibition between the primary sleep (VLPO) and wake centers (rostral RF).
Sleep Disorders and Treatments

Sleep disorders fall (primarily) into one of two complementary categories:

- **insomnia** (disorders of sleep initiation and maintenance); and
- **hypersomnia** (disorders of excessive daytime sleep or sleepiness; e.g., narcolepsy – thought to be due to an orexin deficiency)

Treatments:

**Hypnotic** drugs (benzodiazepines; Valium, Librium) increase sleep time by enhancing the effect of the inhibitory neurotransmitter GABA in the brain
- mode: depress wakeful centers
- complications: tolerance, addiction, cessation leads to insomnia

**Antihypnotic** drugs (stimulants, tricyclic antidepressants) decrease sleep time by increasing the activity of catecholamine transmitters (norepinephrine) by enhancing release and/or blocking reuptake
- mode: mimic wakeful center activity
- complications: lost appetite, addiction

**Chronobiotic** drugs increase sleep time by increasing the level of melatonin
- mode: depress SCN
- complications: drowsiness

**Therapeutic opportunities** drugs that target orexin; few on the market
- mode: agonist (decrease sleep)
- mode: antagonist (increase sleep)